FORMULATION OF PELLETS EMPLOYING EXTRUSION SPHERONIZATION TECHNIQUE AND USING NATURAL EXCIPIENT FOR PEPTIC ULCER TREATMENT

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FORMULATION OF PELLETS EMPLOYING EXTRUSION SPHERONIZATION TECHNIQUE AND USING NATURAL EXCIPIENT FOR PEPTIC ULCER TREATMENT

ABSTRACT

Peptic ulcer is very common problem nowadays for which smoking, stress, use of non-steroidal anti-inflammatory drugs and helicobacter pylori etc are some of the common causes. For the treatment of ulcer drugs like antacids, H_2 blockers, proton pump inhibitors are used which has their own advantages and drawbacks. In this study pellets for the treatment of ulcer will be prepared using extrusion spheronization technique. In formulation of pellets some key excipients like microcrystalline cellulose which acts as spheronising agent and binders like polyvinyl pyrrolidine are used. These excipients can be replaced with some natural excipients like tamarind kernel powder and this study is focusing on finding better alternative to these excipients. Additionally some studies also suggested the use of tamarind against ulcer which will be added benefit in this case, which will also be evaluated. The pellets will be prepared using extrusion spheronization technique with natural excipients. Some of the critical process parameters and some of the key formulation parameters will be analyzed using factorial design. Prepared pellets will be evaluated for various parameters like flow properties, particle size, hardness, drug content, disintegration time, drug release, stability studies etc. The optimized pellet formulation will be compared with marketed formulation for its effectiveness.

Keywords: *Peptic ulcer, Pellets, Extrusion-spheronization, Tamarind Kernel Powder*

OUTLINE OF THE PROPOSED RESEARCH WORK

I. Title of the Research Work:

Formulation of pellets employing Extrusion Spheronization technique and using natural excipient for peptic ulcer treatment.

II. Importance/Rationale of Proposed Investigation:

Peptic ulcer occurs in that part of the gastrointestinal tract (GIT) which is exposed to gastric acid and pepsin, i.e. the stomach and duodenum. An ulcer in the stomach is known as a gastric ulcer while that in the first part of the intestine is known as a duodenal ulcer.

For ***Proton-pump inhibitors (PPIs)*** the gastric H, K-ATPase is the primary target for the treatment of acid-related diseases. PPIs produce long-lasting reduction of gastric acid production.

Pelletization is the process of agglomeration in which mixture of fine powders or granules of bulk drugs and excipients is converted into small, free-flowing, spherical or semi-spherical units, which are called as pellets. Typically size of these pellets varies from 0.5-1.5 mm. As a drug delivery system pellets have both therapeutic and technological advantages which include less irritation of the gastro-intestinal tract, dose dumping, better flow properties, particle size distribution etc.

The ***extrusion-spheronization*** technique which was first reported by Reynolds (1970) is the most popular method of producing pellets. In the preparation of pellets firstly wet mass is prepared which is known as granulation, then prepared wet mass is converted into cylinder like extrudate which is known as extrusion. The extrudate produced are then processed for spheronization where they get converted into spheres/pellets and finally these pellets are dried.

Various Excipients such as Filler (Microcrystalline cellulose), Binder (Polyvinylpyrrolidone), Lubricant (Magnesium stearate) Separating agent (Talc), Disintegrant (Croscarmilose sodium), pH adjuster (Citrates, Phosphates), Surfactant (Sodium lauryl sulphate), Spheronization enhancer (Microcrystalline cellulose) and Release modifier (Ethylcellulose) are used in pellet formulation among which Microcrystalline cellulose is very important excipient.

Tamarind, commonly known as Imli, is a rich source of gum which came into commercial production in 1943 as a replacement for starch in cotton sizing in Indian textile market. The composition of tamarind kernel powder, the source of gum resembles cereals with 12.7-15.4 % of protein, 37.5 % of oil, 7-8.4 % of crude fiber, 61-72.2 % carbohydrates, and 2.45-3.3% of ash.

Pharmaceutical application of tamarind kernel powder are Suspending agent in suspension, Drug release retardant in sustain release tablet, Sustain release spheroids, Microspheres, Tablets, Mucoadhesive tablet, Mucoadhesive patches, Solid dispersion, In situ gel.

- Usage of natural excipient such as tamarind kernel powder has benefits such as reduced cost of finished product such as pellets and tablets.
- One excipient can be good alternative for both spheronising agent and binder used in pellet formulations which aspect is not yet evaluated by any researcher.

III. Scope of Proposed Investigation:

- Proposed investigation will give us idea about concentration tamarind kernel powder which can be used as both spheronising agent and binder in pellet formulations.

- It will further draw attentions towards usage of natural excipients in pellet and tablet formulations on commercial basis.
- As waste material is utilized as excipient for preparation of pharmaceutical product, it will give economical support to concerned farmers.

IV. Location:

Organization/Department where the work is to be done:

- D Y Patil University Pune &
- ACS'S College of Pharmaceutical Science & Research, Ashti

V. Research gaps identified in the proposed field of investigation:

- Tamarind kernel powder is not utilised as spheronising agent and binder in any of the research came accross.
- It is studied for its properties like mucoadhesive, gelling agent, release modifier etc
- Hence no sufficient or extensive work done in proposed field of investigation hence lacks in its utilization on commercial basis.

VI. Objective of the proposed study

- To develop an optimized pellet formulation using natural excipient such as tamarind kernel powder employing extrusion-spheronization technique.
- To perform enteric coating on optimized pellet formulation using enteric coating polymer such as Eudragit
- To perform microbial testing of natural excipient and stability study of formulation to ensure its safety.

VII. Review of Work done on the Subject:

1. **Veravaet C et al. (1994)** review article dealt with the aspects of the extrusion-spheronisation process
2. **Maravaniya PJ et al. (2013) r**eviews the potential advantages, desirable properties of pellets
3. **Eerikiinen S et al. (1991)** suggested that Microcrystalline Cellulose gives best results as spheronising agent.
4. **Wan LSC et al. (1992)** suggested combination of speeds in the range of 1000 – 2000 rpm and residence time between 5 – 15 min to yield pellets of Microcrystalline Cellulose in the size range of 0.7 to 1.0 mm
5. **Sousa JJ et al. (1996)** suggested that physical properties and dissolution profile of the pellets is greatly affected by amount of water used and the drying time.
6. **Podczeck F et al. (2014)** concluded from their study that if extrudate are kept as it is prior to spheronization for some specific time it may affect the properties of pellets and additionally the speed of rotation of the spheroniser plate also greatly affect the properties of the pellets.
7. **Jain KS et al. (2006)** review summarizes various disorders associated with increased gastric acid secretion and various therapeutic strategies to control them
8. **Shin JM et al. (2008)** Pharmacology of proton pump inhibitors
9. **Radha GV et al. (2013)** studied methods of extraction, characterization and applications of tamarind seed polysaccharide
10. **Shaikh SS et al. (2015)** deals with the modification of tamarind kernel powder in order to improve the physicochemical properties.
11. **Kulkarni GT et al. (2005)** for the preparation of Diclofenac sodium spheroids by extrusion spheronization technique they used Tamarindus indica release modifier
12. **Jangdey MS *et al*. (2014)** developed sustained released tablet using tamarindus indica gum
13. **Min Han et al (2018)** Eudragit used for enteric coating of pantoprazole sodium pellets

VIII. Research methodology:

- **Hypotheses to be tested:** Partial or Complete replacement of conventional spheronizing agents like Microcrystaline Cellulose and binders like Polyvinyl Pyrrolidine in pellets by using natural excipient such as tamarind kernel powder.

  Usage of Eudragit for the enteric coating of pellets.

- **Sources of Information:** Research/Review articles from Science Direct, Reference books, Official books, Google, Seminar, Conferences Etc

- **Tools and Techniques of Research:**
  1. **For characterization and compatibility study of drug and excipients:** Infra-Red spectroscopy, UV-Spectrophotometer, Differential scanning calorimetry, X-ray diffraction, Scanning electron microscopy, Brookfield Viscometer etc
  2. **For preparing pellets by extrusion-spheronising technique:** Extruder and Spheronizer
  3. **For evaluation of prepared pellets:** Dissolution & Disintegration, Infra-Red spectroscopy, UV-Spectrophotometer, Differential scanning calorimetry, Scanning electron microscopy, Digital hardness tester etc
  4. **For enteric coating of pellets:** Fluidized Bed Dryer

- **Plan of Work:**

A) Semester wise tentative plan:

1. **Sem-I:** Literature survey
2. **Sem-II:** Outline of work to be done, Procurement of required material, start of research work-characterization of excipients & drugs, compatibility study, initial batches
3. **Sem-III & IV**: Application and preparations of batches as per factorial design, evaluation of batches, optimized batch, enteric coating of optimized pellets and its evaluations.
4. **Sem-V:** stability studies, Comparison of optimized batch with marketed formulations

5. **Sem-VI:** Thesis writing, Finalization of thesis, Evaluation of thesis, Viva

B) Detail plan of work:

1. Literature survey
2. Selection of drug candidate and excipients
3. Procurement of drug and excipients for the preparation of pellets
4. Characterization of drug
   - ✓ Physical properties
   - ✓ Micromeritic properties
   - ✓ Melting point
   - ✓ Fourier transform infrared (FT-IR) spectroscopy
   - ✓ λ_{max} and calibration curve by UV spectrophotometry
   - ✓ Differential scanning calorimetry (DSC)
5. Characterization of excipients
   - ✓ Micromeritic properties of excipients and tamarind kernel powder
   - ✓ FTIR spectroscopy
   - ✓ Physical properties
   - ✓ DSC
   - ✓ Scanning electron microscopy (SEM)
   - ✓ X-ray diffraction (XRD)
6. Compatibility study of drug and excipients
   - ✓ FTIR spectroscopy
   - ✓ DSC
7. Formulation of pellets
   - ✓ Formulation of blank pellets by extrusion- spheronization technique
   - ✓ Formulation of drug loaded pellets by extrusion- spheronization technique
   - ✓ Optimization of formulation and process parameters using factorial design
   - ✓ Formulation of enteric coated pellets from optimized formulation.
8. Evaluation of pellets
   - ✓ Yield
   - ✓ Flow properties
   - ✓ Particle size

- ✓ Hardness
- ✓ SEM
- ✓ DSC
- ✓ XRD
- ✓ Drug content
- ✓ Disintegration time
- ✓ Drug release

9. Comparison of drug release between optimized formulation and marketed formulation

10. Stability studies of optimized formulation

IX. Expected outcome of research: Superior, comparatively low cost finished product (pellets) compare to marketed formulation due to use of natural excipient.

X. Tentative Chapterization

1. Introduction
2. Literature Review,
3. Need of the Work,
4. Aim and Objectives,
5. Plan of Work,
6. Drug and Excipient Profile,
7. Material and Equipments,
8. Experimental Work,
9. Results and Discussion,
10. Summary and Conclusion,
11. References

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